Press release

SAKK/RTFCCR/Gateway Research Grant: Winning studies announced

USD 1,500,000 for cancer researchers in Switzerland and Spain

Five researchers were awarded with the SAKK/RTFCCR/Gateway Research Grant endowed with a total of USD 1,500,000 at the semi-annual meeting of the Swiss Group for Clinical Cancer Research (SAKK). The grant will support the scientists to address five critical challenges and advance clinical cancer research for novel treatment options.

Zurich, 26 November 2015 – The 2015 SAKK/RTFCCR/Gateway Research Grant has been awarded to five different research projects addressing pivotal challenges in clinical cancer research today. This joint research grant is being awarded for the third year by the Swiss Group for Clinical Cancer Research (SAKK), Rising Tide Foundation for Clinical Cancer Research (RTFCCR) and the U.S.-based non-profit organization, Gateway for Cancer Research (Gateway). Founded in 2011, this strategic partnership seeks to accelerate innovative and relevant oncology research that may lead to more potent, less toxic and potentially life-saving treatment options for cancer patients.

Eveline Mumenthaler, Director of RTFCCR, presented the grant awards to the winners during the semi-annual meeting of SAKK in Zurich. This included Dr. Sacha Rothschild, MD, Basel University Hospital, PD Dr. Nicholas Mach, MD, Geneva University Hospital, Prof. Adrian Ochsenbein, MD, Inselspital Bern, Monica Ruggeri of the International Breast Cancer Study Group (IBCSG) Coordinating Center in Bern and Dr. Jordi Rodón, Vall d'Hebron University Hospital in Barcelona, Spain.

“Cancer remains a worldwide health problem. With over 100 different known cancers that affect humans, factors such as an aging population together with the evolution of lifestyle continue to make cancer a major societal challenge. While new discoveries have brought about innovative diagnostic approaches and effective therapies, a continuous strong financial support is required to advance novel and evidence-based research. This is why we are enthusiastic about the prospects of our third-year of grant partnership with SAKK and Gateway, which increased from 450’000 USD for one project to USD 1,500,000 for five projects,” said Eveline Mumenthaler.

Beat Thürlimann, President of the SAKK, is especially delighted that the grant endowment has been increased to mark the SAKK's 50th anniversary in 2015 and that research in a number of categories is eligible for support: "The aim of the grant is to support five academic research projects. This is entirely in keeping with the SAKK's mission. As an academic research institute, we have been committed for the past 50 years to finding the best possible cancer therapy for patients in Switzerland."

Scientists applying for the research grant were able to submit their projects in five categories: increasing the efficacy of cancer diagnostics and therapeutics through targeted and personalized medicine; development of approaches for metastatic disease; overcoming drug resistance; improving quality of life; and use of repurposed drugs. All submissions were

reviewed in a two-stage process by an international committee comprising scientific experts from SAKK, RTFCCR and Gateway. The final decision was reached in October 2015.

In previous years, two research grants endowed with 450'000 USD each, were awarded to Prof. Dr. Christoph Driessen, Cantonal Hospital St.Gallen, in 2013 for his phase II, multicenter clinical trial for myeloma and Prof. Dr. Radek Skoda, University Hospital Basel, in 2014 for his clinical study focused on creating a novel treatment option for bone marrow cancer patients without therapy alternatives.

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Rising Tide Foundation for Clinical Cancer Research (RTFCCR) *is a private non-profit organization established in 2010 in Switzerland. It actively seeks the brightest minds in science and medicine, and collaborates with a global network of research excellence centers to fund novel, highly promising clinical trials and translational research that can improve patients' survival and quality of life within 3 years or less. For more information: www.risingtide-ccr.com*

Gateway for Cancer Research *is a U.S. based nonprofit 501(c)(3) organization committed to funding innovative and meaningful cancer research studies that help people living with cancer to feel better, live longer and conquer cancer TODAY! Thanks to generous underwriting by Cancer Treatment Centers of America®, 99 cents of every dollar Gateway receives directly funds phase I and phase II cancer clinical trials at leading research institutions around the world. Since 1991 Gateway has supported more than 140 clinical trials and funded millions in leading-edge research, including blending the best of conventional, and complementary and alternative therapies. Get involved today by visiting GatewayCR.org, like us on Facebook at facebook.com/demandcures and join the conversation on Twitter @DemandCures, #BeAGateway.*

The ***Swiss Group for Clinical Cancer Research (SAKK)*** *is a non-profit organization, which has been conducting clinical trials in oncology since 1965. Its primary objective is to research new cancer therapies, to develop existing treatments further and to improve the chances of a cure for patients with cancer. This takes place through cooperative projects within Switzerland and in collaboration with centers and study groups abroad. The SAKK is supported by a service-level agreement with the State Secretariat for Education, Research and Innovation (SERI) and also by partners such as the Swiss Cancer League and Swiss Cancer Research. For more information, go to www.sakk.ch*

The award-winning research projects

Category 1 - Increase the efficacy of cancer diagnostics and therapeutics through targeted and personalized medicine

Dr. Sacha Rothschild, MD PhD, Basel University Hospital, Medical Oncology and University of Basel, Department Biomedicine, Laboratory for Cancer Immunology

Treatment concept including immunotherapy for improved care of lung cancer patients

Lung cancer is the most frequent malignant tumor. Non-small cell lung cancer (NSCLC) accounts for 80% of all lung cancer cases. One fourth of patients are diagnosed with locally advanced disease with involvement of regional lymph nodes (UICC stage IIIA). This stage is amenable to a curative treatment approach; however the outcome is still poor with half of patients suffering from a relapse in the first year after therapy. Our research group established the use of preoperative chemotherapy (3 cycles of cisplatin and docetaxel) followed by tumor resection as the standard of care for this patient population.
Cancer immunotherapy is attracting increasing attention as a viable therapeutic option, and is now regarded as the fourth cornerstone of anticancer treatment. Immuno-modulatory antibodies targeting the PD-1/PD-L1 axis such as MEDI4736 have shown striking response rates in pre-treated patients with different cancer types including lung cancer.
In view of the previous SAKK trials (SAKK 16/96 and SAKK 16/00) and the current international knowledge of stage IIIA (N2) disease it is hard to envision a serious break-through by changes in one of the classical modalities: surgery, chemo- or radiotherapy. In order to substantially increase the cure rate novel means have to be found. We therefore believe that the addition of the anti-PD-L1 inhibitor MEDI4736 to standard chemotherapy in the neoadjuvant setting has the potential to substantially improve the outcome of NSCLC patients with stage IIIA disease.
Here, we propose translational research projects to flank the clinical trial. The clinical trial with preoperative use of immune checkpoint inhibition allows for extensive analysis of the tumor tissue that is resected afterwards. The translational research projects will allow a deeper understanding of the in vivo mechanisms reflected by immunologic changes in the tumor microenvironment. The planned experiments will allow us to unravel the underlying molecular as well as immunological mechanisms of immune checkpoint inhibitor treatment and provide an accurate immunological definition of changes in the tumor microenvironment. This knowledge is clearly needed to optimally implement these new agents in the armamentarium of anti-tumor agents. The results of our project should help designing new clinical trials with immune checkpoint inhibitors for the benefit of our patients.

Original title: SAKK 16/14 – Anti-PD-L1 antibody MEDI4736 in addition to neoadjuvant chemotherapy in non-small cell lung cancer (NSCLC) patients with mediastinal lymph node metastases (stage IIIA (N2))

Category 2 - Develop approaches for metastatic disease with broad applicability to multiple cancers

PD Dr. Nicholas Mach, MD, Geneva University Hospital

Personalized cell-based immunotherapy using encapsulation cell technology

Many deadly cancer are diagnosed at an advanced stage despite preventive measures. The vast majority of individuals suffering from cancer with local infiltration or metastasis will die from their malignancy within three years despite the currently available therapies. New treatments for advanced malignant cancers are critically needed. In recent years novel anti-tumor immunotherapy strategies have led to interesting clinical benefit in a significant portion of patients with advanced refractory cancers in several tumor types: melanoma, squamous cell lung cancer, bladder cancer, gastric, head and neck cancer. MVX-ONCO-1 is an innovative anti-cancer immunotherapy with unique specificity. Therapy is individualized and can be applied to any cancer type. Every tumor is unique, with its own set of molecular/genetic alterations that generate abnormal proteins. Each anomaly is a potential target (antigen) for an efficient immune system. In addition to the right targets, potent tumor-specific active immunotherapy needs a very strong immune booster, or adjuvant, in order to efficiently stimulate the immune system.
MVX-ONCO-1 is an investigational medicinal product (IMP) that combines patient-specific targets and a potent adjuvant (GM-CSF) in a subcutaneous (sc) formulation. The specific antigens are obtained from the patient's own cancer cells harvested from the primary tumor or a metastasis. The adjuvant is released locally at the vaccine site in a controlled, standardized manner for several days. To fulfill such a requirement, MVX-ONCO-1 uses a small capsule containing a cell-line producing a stable level of the adjuvant protein. Both the capsule and the patient's inactivated cells are implanted in normal skin. In animal models, protective, specific and long-lasting anti-tumor immunity has been observed in every cancer type when inactivated tumor cells, genetically modified to produce GM-CSF, are implanted sc. A first in humans, a Phase 1 clinical trial has recently been completed. With initial data showing a very good safety/feasibility profile and some interesting clinical activity, the SAKK/RTFCCR/Gateway Research Grant will allow the evaluation of MVX-ONCO-1 in a multicenter, Phase 2 efficacy study in Switzerland. MVX-ONCO-1 is the first personalized cell-based immunotherapy using encapsulation cell technology. The development of innovative anti-tumor strategies with limited toxicity that are potentially applicable to many cancer types achieves one of the goals of the Foundation.

Original title: Personalized, cell-based antitumor immunization with MVX-ONCO-1, a combination of subcutaneous irradiated autologous tumor cells and encapsulated allogeneic cells engineered to release GM-CSF: a single arm Phase II trial

Category 3 - Develop technologies or therapeutic approaches to overcoming drug resistance of refractory cancers

Prof. Adrian Ochsenbein, MD, Inselspital Bern

New combination therapy for elderly and frail patients with newly diagnosed acute myeloid leukemia

Leukemia stem cells are resistant to most available treatment options including chemotherapy. We showed in preclinical studies that targeting CD70, a molecule that is expressed on blast and stem cells of acute myeloid leukemia (AML), can eliminate leukemia stem cells. In this clinical study we will combine a standard treatment for AML, azacytidine, with an antibody that specifically targets CD70-expressing cells (ARGX-110). Azacytidine reduces blast cells in AML but does not eliminate the leukemia stem cells. Our data show that both treatments act synergistically to target the disease-initiating stem cells. The goal of the study is to assess the safety of the combination therapy and its effect on leukemia stem cells.

Original title: A phase I open-label, dose-escalating study with expansion cohort to evaluate safety and tolerability of ascending intravenous doses of ARGX-110 in combination with azacytidine in patients with newly diagnosed acute myeloid leukemia (AML) and high-risk myelodysplastic syndrome

Category 4 - Improve quality of life: a) new curative approaches with immediate impact on the quality of life of patients; or b) address late effects and long-term outcomes of cancer therapies

Monica Ruggeri, IBCSG Coordinating Center, Bern

Safety of interrupting endocrine therapy for young women with endocrine responsive breast cancer who desire pregnancy

Young women faced with breast cancer are often concerned about treatment-related fertility impairment as many of them were unable to complete their family planning before diagnosis. A significant proportion of women take into account the risk of infertility when discussing cancer treatments with their health professionals. All available data about the safety of pregnancy after breast cancer are reassuring but only retrospective and limited evidence is available in women with endocrine-responsive disease who, for age-related or personal reasons, wish to attempt pregnancy early after diagnosis. In addition, long-term (5-10 years) post-operative endocrine therapy could reduce the possibility of subsequent pregnancies in many of these women. The International Breast Cancer Study Group (IBCSG) is conducting a clinical trial (IBCSG 48-14/BIG 8-13 POSITIVE) to assess the safety and outcome of pregnancy in young women with endocrine-responsive breast cancer, within a collaboration across all continents. The trial allows, after 18-30 months of endocrine therapy, up to a 2-year treatment interruption to attempt pregnancy, followed by treatment resumption to complete the prescribed 5-10 years. Breast cancer relapse, outcome of pregnancy and birth health will be assessed. A total of 500 patients are planned to be recruited in different regions of the world in approximately four years. The POSITIVE trial is an innovative and unique approach in breast cancer care, designed to provide important, prospective, scientifically sound evidence regarding the safety

of pregnancy in these young patients, who face breast cancer in a sensitive period of their lives.

Original title: IBCSG 48-14 POSITIVE: A study evaluating the pregnancy outcomes and safety of interrupting endocrine therapy for young women with endocrine responsive breast cancer who desire pregnancy

Category 5 - Use of repurposed drugs and devices to quickly find safe and affordable treatments for both common and rare disorders.

Dr. Jordi Rodón, Vall d'Hebron University Hospital, Barcelona

Assess the anti-tumor effect of the antihelminthic agent ivermectin

The IVINCA clinical trial aims to test the anti-tumor effect of ivermectin in a clinical setting. If clinical tests are successful, we propose the repurposing of this drug as a cancer therapy. As far as we know, this has never been tested before. Ivermectin is a highly effective antihelminthic agent used in veterinary and human medicine. It was first approved for human use in 1987 and developed by Merck, Sharpe and Dome & Co. (MSD) as Mectizan® for the treatment of onchocerciasis, lymphatic filariasis, strongyloidosis and scabies and river blindness caused by onchocerca.
An active canonical WNT pathway has been linked to poorer survival and incurable metastatic disease in a number of patients presenting with advanced colorectal cancer, endometrial cancer and other tumors. The purpose of this study is to clinically assess the anti-tumor effect of ivermectin in patients with these molecular alterations. Specifically, we will determine 1) whether the proposed treatment is effective against those tumors presenting alterations in the WNT-TCF pathway and 2) the safety of the drug candidate. We have strong preclinical evidence that justifies the design of a clinical trial. However, studies in the laboratory have shown that not all advanced and metastatic colorectal cancers respond to blockade of WNT-TCF. The key and essential aspect of this trial is the identification of the safe dose in chronic treatment and determination of which patients will respond to ivermectin and which will not. For this reason, this clinical study has also been designed to identify pharmacodynamic biomarkers as a preliminary step in the development of predictive and/or prognostic biomarkers for a clinical response to ivermectin treatment.
The innovative use of ivermectin as a WNT-TCF pathway response inhibitor affords the opportunity to use an already available drug that can more significantly target this pathway than any other WNT inhibitor in development. Moreover, it will be an important source of information for the scientific community because WNT-TCF is a relatively novel target, no diagnostic system is in place to detect its alteration in patient samples, and there is an unmet need in the clinical setting for drugs that inhibit the WNT-TCF pathway.

Original title: IVINCA trial (IVermectin IN CAncer), a trial of ivermectin as an anticancer WNT-TCF response inhibitor